RE MARKS

I. Status of the Claims

Claims 1-36 were originally filed. Claims 1-13, 16, and 28-36 have been canceled. Upon entry of the present amendment, claim 14 is amended to recite that "the vanadium haloperoxidase polypeptide comprises an amino acid sequence having at least 90% sequence identity to the sequence from residue 435 to residue 632 of SEQ ID NO:2." Claim 17 is amended to recite a 95% sequence identity. These sequence identity percentages are supported by the specification, *e.g.*, on page 8, lines 7-12. Claims 17-21, 23, and 27 are further amended to correct improper claim dependency due to the cancellation of claim 16. Claims 14, 15, and 17-27 are currently pending.

II. Claim Rejections

A. 35 U.S.C. §112, Second Paragraph

Claim 17-24 and 27 were rejected under 35 U.S.C. §112, second paragraph, for indefiniteness because they depend from the canceled claim 16. The present amendment has cured all improper claim dependency. Applicant submits that the indefiniteness rejection is obviated.

B. 35 U.S.C. §112, First Paragraph

Written Description

Claim 14, 15, 25, and 26 were rejected under 35 U.S.C. §112, first paragraph, for alleged inadequate written description. Applicant respectfully traverses the rejection in light of the present amendment.

To satisfy the written description requirement, a specification must describe the claimed invention in sufficient detail such that one of skill in the art can reasonably conclude that the inventor had possession of the claimed invention. Possession of claimed invention may be shown by a variety of descriptive means, including words, structure, figures, diagrams, and

formulas. MPEP §2163 I. Case law provides more specific guidance in setting the standard for written description.

The amended claims are now directed to polypeptides comprising a vanadium haloperoxidase polypeptide. This vanadium haloperoxidase polypeptide has the following features: (1) it consists of a catalytic domain that complexes a vanadium ion and catalyzes the oxidation of ODA; (2) it comprises an amino acid sequence at least 90% identical to the 435-632 segment of SEQ ID NO:2; and (3) it has a molecular weight of no more than 40 kDa. These claims fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993).

On the other hand, proper description of functional features of a claimed invention can also play an important role in satisfying the written description requirement. The Federal Circuit recently stated that "*Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

With regard to the claimed polypeptides, pending claims set forth commonly shared structural features of the claimed polypeptides by providing a percentage sequence identity to a reference sequence (*e.g.*, 435-632 of SEQ ID NO:2). The claimed polypeptides are therefore effectively described structurally. Given the minimal requirement of a 90% amino acid sequence identity, a claimed polypeptide can have no more than 19 amino acids different from SEQ ID NO:2 within the region of 435-632. As described in the specification (see, *e.g.*, last

paragraph on page 27), SEQ ID NO:2 (676 amino acids) is the amino acid sequence of a vanadium peroxidase isolated from *Fucus* and has a significant level of sequence homology to another vanadium peroxidase, isolated from *Ascophyllum* (85.8% identical for the 232 amino acids of the C-terminal sequence and 89% identical for the full length sequence). Thus, once the amino acid sequence of SEQ ID NO:2 is determined, one of skill in the art would be able to compare this sequence with other vanadium peroxidase sequences, such as the one from *Ascophyllum*, and readily determine which amino acids within the region corresponding to 435-632 of SEQ ID NO:2 are likely to be critical for the enzymatic activity and should therefore be preserved, and which other amino acids within that region may not be required for the enzymatic activity and can therefore be modified. In light of the widely available technical skills in the art, the description found in this application can therefore reasonably convince an artisan that the present inventor had possession of a genus of polypeptides, and not just one single species, *i.e.*, SEQ ID NO:2.

Commonly shared functional features of the claimed polypeptides are also provided: each comprises a vanadium haloperoxidase polypeptide that is capable of complexing vanadium ion and catalyzing the oxidation of ODA. These functional features can be readily tested by one of ordinary skill in the art using well established, routinely practiced techniques as well as according to the teaching of the present specification (*see, e.g.*, page 25, lines 17-29, and page 28, line 24, to page 29, line 6). In addition, several exemplary polypeptides of the claimed genus are described in the specification, *see, e.g.*, Figure 3.

Thus, both structural and functional features commonly shared by the claimed genus of polypeptides have been described in detail, and multiple examples are provided, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Such description is consistent with the written description standards set forth in both *Lilly* and *Amgen*.

Applicant believes that the claimed invention within the current claim scope is properly described by the specification under 35 U.S.C. §112 first paragraph. As such, the withdrawal of written description rejection is respectfully requested.

Enablement

Claims 14, 15, 25, and 26 were rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. Applicant respectfully traverses the rejection in light of the present amendment.

A claimed invention is enabled when the disclosure allows one of ordinary skill in the art to make and use the invention without undue experimentation. MPEP §2164.01. The test for enablement as set forth in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), requires the consideration of multiple factors: the breadth of the claims; the nature of the invention; the state of the prior art; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In the present case, the claims are directed to polypeptides comprising a vanadium haloperoxidase polypeptide, which has well-defined structures and readily testable functional features: *e.g.*, consisting of a catalytic domain that complexes a vanadium ion and catalyzes the oxidation of o-dianisidine (ODA); comprising an amino acid sequence having at least 90% sequence identity to the sequence from residue 435 to residue 632 of SEQ ID NO:2; and having a molecular weight of no more than 40 kDa. The claimed genus of polypeptides is therefore not overly broad.

This invention relies on the basic techniques of molecular biology and biochemistry. As the Examiner has acknowledged, the level of technical sophistication is high in the art, which would sufficiently allow one ordinarily skilled artisan to produce a large number of polypeptides within the claimed genus, based on the exemplary vanadium peroxidase sequences disclosed in this application.

The specification contains ample directions to practice the invention, such as methods of cloning and modifying the coding sequences for vanadium peroxidase polypeptides (*see, e.g.*, page 13, line 30, to page 15, line 6; page 19, line 23, to page 21, line 29; and Table 1 on page 22), expression of the polypeptides (*see, e.g.*, page 15, line 10, to page 19, line 21), and enzymatic assays for detecting peroxidase activity (*see, e.g.*, page 25, lines 19-27, and page 28, line 24, to page 29, line 6). More importantly, as discussed above, because of the existence of other related vanadium peroxidases of known amino acid sequences (*e.g.*, one isolated from *Ascophyllum*, described in the last paragraph on page 27), sequence comparison would provide reasonable guidance as to which amino acid residues are likely to be essential for the function of the enzyme and should therefore be preserved, whereas others may not be essential and can therefore be deleted, substituted, or otherwise modified. For these reasons, Applicant respectfully disagrees with the Examiner's assertion that one would be unlikely to succeed in making variants from SEQ ID NO:2 because the specification offers no guidance regarding how to make modifications while retaining the desired enzymatic activity (see middle paragraph on page 6 of the Final Office Action).

While Applicant does not dispute that some polypeptides that possess the described structural characteristics may not retain the catalytic activity of a vanadium peroxidase, such functionally inoperable embodiments can be easily identified and eliminated through enzymatic assays. Vanadium peroxidase activity can be readily tested according to the methods commonly used by those skilled in the art or the methods taught by the specification (*see, e.g.*, description on page 25, lines 19-27, and page 28, line 24, to page 29, line 6). MPEP §2164.01 states, "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." In the present case, the necessary experimentation requires nothing beyond the use of routine techniques, such as modification of a polynucleotide coding sequence, recombinant expression of a polypeptide, and peroxidase activity assays, which is exactly what "the art typically engages in." Thus, the experimentation does not constitute undue experimentation.

Taken together, analysis of the Wands factors and the specific facts in this application indicates proper enablement of the claimed invention. Applicant thus respectfully requests the withdrawal of the enablement rejection.

CONCLUSION

In view of the foregoing, Applicant believes that all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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